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Case report

Pulmonary aspergilloma: A rare differential diagnosis to lung cancer after positive FDG PET scan

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ABSTRACT

Early diagnosis and treatment of lung cancer, one of the leading causes of cancer-related death, is important to improve morbidity and mortality. Therefore any suspect solitary pulmonary nodule should prompt the pursuit for a definitive histological diagnosis. We describe the case of a 55-years-old male ex-smoker, who was admitted to our hospital due to recurrent hemoptysis and dry cough. A CT scan showed an irregular nodule of increasing size (28 mm in diameter) in the left lower lobe (LLL). A whole body PET-CT scan (643 MBq F-18 FDG i.v.) was performed and confirmed an avid FDG uptake of the nodule in the LLL, highly suspicious of lung cancer, without any evidence of lymphogenic or hematogenic metastasis. Bronchoscopy was not diagnostic and due to severe adhesions after prior chest trauma and the central location of the nodule, a lobectomy of the LLL was performed. Surprisingly, histology showed a simple aspergilloma located in a circumscribed bronchiectasis with no evidence of malignancy. This is a report of an informative example of an aspergilloma, which presented with symptoms and radiological features of malignant lung cancer.

1. Introduction

Lung cancer is one of the leading causes of cancer-related death for men and women in industrialized countries. Early diagnosis and treatment is crucial to improve morbidity and mortality. Positron emission tomography (PET) is a quantitative molecular imaging technique that has significantly improved diagnosis, staging and evaluation of treatment options for lung cancer patients. Its sensitivity to detect pulmonary malignancies is about 96% [1]. Nevertheless, a variety of non-malignant, mainly granulomatous, infectious, and inflammatory conditions can also lead to an increased fluorodeoxyglucose (FDG) uptake and may thus mimic lung cancer [2]. Therefore the reported specificity of FDG PET is markedly lower, around 78%, than its sensitivity [1]. Thus, with the growing and more widespread usage of FDG PET scans, an increasing number of less common, non-malignant, but nevertheless PET positive findings, are getting detected. Here we describe the case of a PET positive, irregular pulmonary nodule turning out to be an aspergilloma.

2. Case report

Two years before admission, a 55-years-old male ex-smoker (2 pack years) presented to a peripheral hospital with a history of chronic dry cough and intermittent hemoptysis. A CT scan revealed a solitary nodule (15 mm in diameter) in the left lower lobe (LLL) (Fig. 1 panel A). Subsequent bronchoscopy showed neither any suspect endoluminal lesion nor signs of an active bleeding. The cytological evaluation of the bronchial washing and brushing were both negative for malignant cells, neutrophil granulocytes, macrophages and siderophages. Furthermore no growth of pathogenic agents was seen in microbiological cultures. Due to the history of very low tobacco smoke exposure and a past history of left-sided thoracotomy for evacuation of intrathoracic hematoma after severe chest trauma 40 years ago, thus having the potential for residual intrapulmonary scar tissue, follow-up imaging was recommended by the treating physicians.

The patient was then admitted to our hospital due to another episode of recurrent hemoptysis and dry cough following an acute

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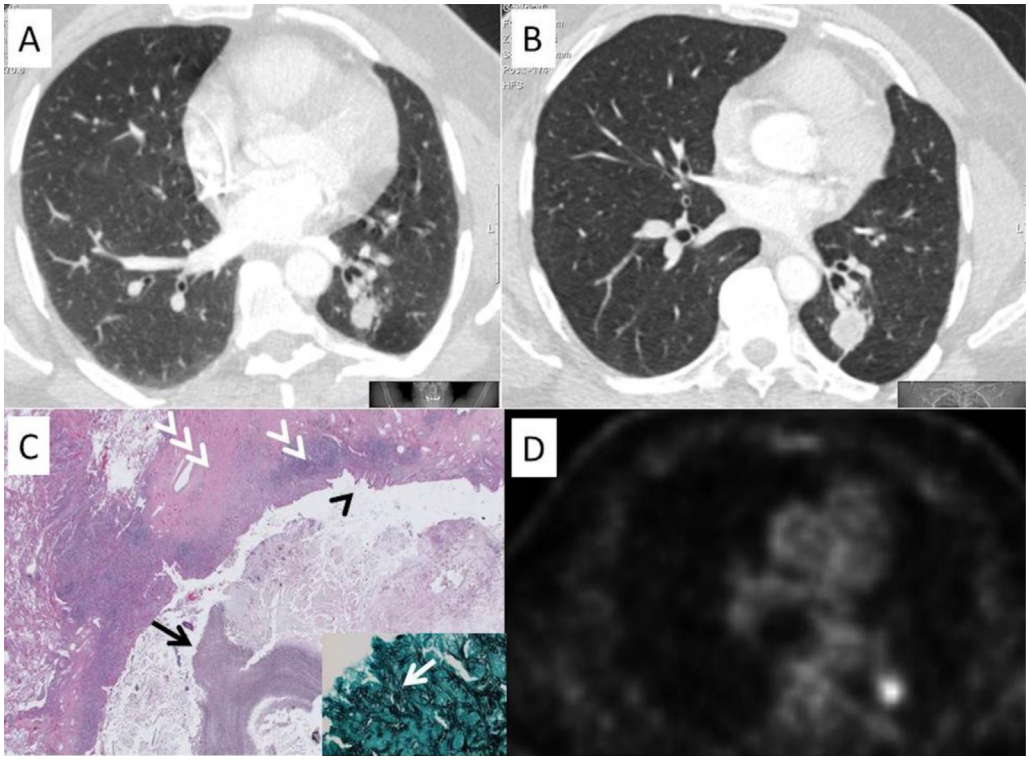

Fig. 1. Panel A: CT scan two years ago showing a solitary, irregular nodule (15 mm in diameter) in the left lower lobe; **Panel B**: Recent CT scan showing an increase of the nodule (28 mm in diameter) 2 years later; **Panel C**: Histology: Part of a large bronchial lumen compared to neighboring alveoli (on the left). The bronchial wall contains a polypoid arranged epithelium (black arrowhead) and a severe up to lymphofollicular (double arrowhead) inflammatory infiltrate in a dense collagen-fibrous stroma (triple arrowhead). The lumen is filled with faint basophilic amorphous mucus and a dark basophilic zone (black arrow) (Hemalaun and Eosin stain, bar 500 μm). Aspergilloma (bottom right): In this zone the inset reveals septated and 3 μm thick fungal hyphae (white arrow) in a dense arrangement, compatible with aspergillus (silvermethenamin stain, bar 10 μm). **Panel D**: FDG-PET scan corresponding to panel B.

lower respiratory tract infection one month before admission. Additionally, he now reported of occasional chest pain since two months. Shortness of breath, fever, night sweats, or weight loss was not present. The recent CT scan showed an irregular nodule of increasing size in the LLL (now 28 mm in diameter) without signs of mediastinal or hilar lymphadenopathy (Fig. 1 panel B). Lung function testing showed a mild restriction without any evidence of obstruction (FEV1 73% predicted, TLC 74% predicted). Routine blood tests showed no pathological results, especially inflammatory markers, i.e. C-reactive protein and white blood count, were within normal values. A whole body PET-CT scan (643 MBq F-18-FDG i.v.) was performed and confirmed an avid FDG uptake of the nodule in the LLL, highly suspicious of lung cancer, without any evidence of lymphogenic or hematogenic metastasis (Fig. 1 panel D). Since bronchoscopy was not diagnostic and the nodule was not accessible for CT guided biopsy due to its central location, the patient was transferred to the department of thoracic surgery to obtain a definitive histological diagnosis. Due to severe adhesions after prior chest trauma and thoracotomy and due to the central location of the nodule, a complete lobectomy of the LLL had to be performed. Surprisingly, histology showed a simple aspergilloma located in a circumscribed bronchiectasis with no evidence of malignancy (Fig. 1, panel C). The postoperative course was uneventful and up to now, 2 years after the operation, the patient is free of any pulmonary signs and symptoms.

3. Discussion

Our case of an aspergilloma is an interesting example of an unexpected histological result of a PET-positive, progressing nodule, highly suspicious of lung cancer. Aspergilloma, also known as mycetoma or “fungus ball”, is associated with the growth of fungus (mainly *Aspergillus* species) and usually develops in preformed cavities, commonly in pulmonary emphysema bullae or residual cavities following abscessing infections. *Aspergillus fumigatus*, the most common species together with *Aspergillus flavus* and *Aspergillus niger*, is typically inhaled as small (2–3 μm) spores and settles in a preformed cavity of the lungs, where it grows free, multiplies and forms a fungus ball, usually without tissue infiltration. Thus the typical radiological feature of an aspergilloma is a round to oval solid mass, which is separated from its cavity wall by an airspace of variable extent (“air crescent sign”). Beside the typical Aspergilloma, there is a wide spectrum of Aspergillus-related pulmonary diseases that all can mimic symptoms, signs and radiological features of lung cancer [3,4].

Chronic pulmonary aspergillosis is a progressive and destructive pulmonary infection, which is usually associated with underlying pulmonary pathologies (e.g. mycobacterial infection, emphysema, sarcoidosis or even trauma) that may lead to formation of cavities, bullae or scarring in the lungs [5]. Diagnosis includes the demonstration of specific Aspergillus IgG antibodies or positive respiratory cultures together with the presence of radiological features and non-specific symptoms, such as dyspnea, cough, weight loss and fever. Hemoptysis is a frequent complication and can be life threatening. The prevalence of concomitant positive Aspergillus antibodies or Aspergillus cultures in lung cancer is unknown, furthermore lung cancer and aspergillosis may be present simultaneously and impede the diagnosis of multiple lesions difficult. Moreover many patients with lung cancer have emphysema, which is one of the most common underlying conditions for pulmonary aspergillosis [6].

On the other hand tumors of low activity (e.g. carcinoid tumors or metastases of tumors with a mucinous component) or small

tumor size (e.g. lesions that are smaller than 1 cm may not show high FDG uptake because of the 1-cm resolution of PET systems) are major causes of false negative findings on PET scans. For example, lepidic adenocarinoma can typically be a potential causes of false negative findings on FDG PET scans because of mild degrees of atypism, mitosis and desmoplasia with lower peak SUVs than those of other lung carcinomas [2]. Knowledge of the differential diagnosis that can mimic lung cancer on PET scans is important to ensure early diagnosis and treatment of the underlying disease and to exclude lung cancer.

In conclusion, our case is an informative example of an aspergilloma, which presented with symptoms and radiological features of primary lung cancer, including increasing size and a highly suggestive positive PET scan. The prevalence of chronic pulmonary aspergillosis is unknown and most likely depends on the prevalence of underlying pulmonary diseases. In our patient, a circumscribed bronchiectasis, that was visible allusively on the initial CT scan two years ago, and may even be caused by the severe chest trauma with presumed laceration of the lung 40 years ago, was the starting point for the development of an aspergilloma.

However, any suspect solitary pulmonary nodule should always prompt the pursuit for a definitive histological diagnosis.

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